Nesiritideは安全だが有益性は乏しいことが示された（Abstract＃21828）

ASCEND-HF：重症心不全患者を対象とした大規模スタディの結果、nesiritideは安全であるが症状または死亡率に対する有意な有益性はないことが示された

ASCEND-HF: Large study of patients with severe heart failure confirms nesiritide safe, but shows no significant benefit on symptoms or mortality

大規模臨床試験において、急性非代償性心不全患者に対し薬剤nesiritideは安全であることが証明されたが、呼吸困難に対しては有効性がわずかであり、再入院または死亡率に対する有意な効果はないことが示されたとのレイトブレイキング臨床試験の結果が2010年AHA学会で発表された。急性非代償性心不全におけるnesiritideの臨床上の有効性に関する試験（Acute Study of Clinical Effectiveness of Nesiritide in Decompensated Heart Failure Trial：ASCEND-HF）において研究者らは急性重症心不全患者7,141人（平均年齢67歳、女性34%）を静脈内nesiritide持続投与またはプラセボ投与のいずれかを標準的な治療法に加えて投与する群に無作為に割り付けた。半数以上（60%）が冠動脈疾患を有していた。治療6時間後に nesiritideはプラセボと比較し息切れをやや改善させ、有意な改善はnesiritide群患者の947人（15.0%）に、プラセボ群では874人（13.4%）に認められた。同様に、治療24時間後に呼吸機能が著明に改善した患者はプラセボよりもnesiritide群において多かった－nesiritide群患者のうち1,063人（30.4%）であったのに対しプラセボ群患者では966人（27.5%）であった。しかし、呼吸困難に関する事前に特定していたエンドポイントに関しての有意差はなかった。この薬剤は30日間の再入院または死亡（nesiritide群9.4%対プラセボ10.1%）に関しても有意差は示さなかった。

Full Text

In a large clinical trial, the drug nesiritide proved to be safe but had little effect on dyspnea, and no significant effect on hospital readmission or death rates among patients with acutely decompensated heart failure, according to late-breaking clinical trial results presented at the American Heart Association's Scientific Sessions 2010.

In the Acute Study of Clinical Effectiveness of Nesiritide in Decompensated Heart Failure Trial (ASCEND-HF), researchers randomized 7,141 patients with acute, severe heart failure to receive either continuous intravenous nesiritide or a placebo, both added to standard therapy, which includes diuretics, morphine and other medications.

Six hours after treatment, nesiritide slightly improved shortness of breath compared with placebo, with significant improvement occurring in 947 nesiritide patients (15.0 percent) and 874 placebo patients (13.4 percent). Similarly, 24 hours after treatment, more patients on nesiritide displayed markedly improved breathing function compared to placebo - 1,063 nesiritide patients (30.4 percent) compared to 966 placebo patients (27.5 percent). However, there was no significant difference in the pre-specified endpoint for dyspnea. At 30 days post-treatment, the rates of death from any cause and hospital readmission for heart failure were slightly lower with nesiritide compared to placebo. At 9.4 percent versus 10.1 percent, however, the difference in these rates was not statistically significant either.

Nesiritide is a manufactured drug derived from a naturally occurring protein known as human B-type natriuretic peptide. The drug helps to relax the blood vessels, which can improve circulation, and increase the body's output of excess salt and water.

"Nesiritide was marketed and widely used in the U.S. because of a perception that it had a major effect on dyspnea and then largely abandoned in clinical use because of concerns that it might increase rates of death and renal failure, said Robert M. Califf, M.D., study chair and vice chancellor for clinical research at Duke University School of Medicine in Durham, N.C. "Now that we finally have a proper clinical trial we know that both perceptions were incorrect; nesiritide is safe but has only a modest effect on dyspnea. This is a major signal that we must do a better job defining the biological effects of drugs early in development and conduct adequately powered outcomes trials much earlier to give doctors and patients the necessary information to enable appropriate use of the treatment in practice."

ASCEND-HF, a randomized double-blind trial, included participants from 400 international centers in 30 countries. Average age of patients studies was 67 years, 34 percent were female and 15 percent were African American. More than half (60 percent) had blockages or narrowing of the blood vessels supplying the heart. Treatment began within 24 hours of hospitalization for worsening symptoms and continued for between one to seven days. The study ran from May 2007 to September 2010; patients were followed for 30 days.

Previous studies have shown that nesiritide can relieve shortness of breath if given within three hours of the onset of worsening heart failure, but it was unclear whether this improvement persisted. Also unknown was whether nesiritide caused renal impairment or increased the risk of death, which previous, much smaller studies have indicated. An important finding from this trial is that the drug did not increase these risks.

"I think the main message is that we need to do adequately powered studies to really understand the balance of safety and effectiveness," said Adrian F. Hernandez, M.D., co-investigator of the trial and associate professor of medicine at Duke University School of Medicine. "Now that we've done an adequate trial, we know that nesiritide can be used safely, but there is no mandate to use it because of its modest effects."

"ASCEND-HF represents an important milestone in our understanding of acute heart failure care as this is the first robust drug safety study completed in this difficult to treat patient population," said Christopher M. O'Connor, M.D., the study's co-principal investigator and director of the Duke Heart Center. "Given the complexities of heart failure, there is a significant need for better medications for use in treatment," said Randall C. Starling, M.D., study co-investigator and head of the section of Heart Failure and Cardiac Transplant Medicine and vice chairman of Cardiovascular Medicine at Cleveland Clinic. "With the safety questions related to nesiritide having now been addressed, it could be an option for physicians depending on their interpretation of clinical benefit."

The trial was led by an international executive committee which also included Paul W. Armstrong, M.D.; Kenneth Dickstein, M.D.; Daniel Gennevois, M.D.; Vic Hasselblad, Ph. D.; Michael Komajda, M.D.; Barry Massie, M.D.; John J.V. McMurray, M.D.; Markku Nieminen, M.D.; Jean L. Rouleau, M.D.; and Karl Swedburg, M.D. ASCEND-HF was coordinated by the Duke Clinical Research Institute led by Craig J. Reist, Ph.D. Author disclosures are on the abstract.

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Cardiology特集

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